Shedding light on active species in Fe, Ni and Cu catalysis

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Summary

Many of the transformations that chemists struggle with in the laboratory are often carried out by nature with better activity, selectivity and with bio-degradable waste. In sharp contrast to biological systems, manmade structural and functional models of biological systems usually suffer severely from a lack of reactivity and selectivity in their catalytic reactions. Matching the capabilities of biological systems with mimics in the laboratory is a seemingly impossible task. In biological systems complex structures are involved in chemical reactions, for example enzymes, where chemical reactions are carried out at a so called active site. Apart from the active site, the remaining part of the protein provides a second coordination sphere, which helps to achieve better selectivities towards chemical reactions by allowing the substrate to enter into the active site preferentially in only one orientation. These advantages are not readily available to biomimetic systems. However, in a few biomimetic systems a controlled second coordination sphere environment has been created successfully.[1] One such system is the topic of chapter 8, however, albeit that the catalytic reactions are not discussed there. In this thesis a number of biomimetic systems including the Fe^{II}-N4Py group of complexes (Figure 1), which are functional mimics for Fe^{II}-BLM (BLM = bleomycin) (chapter 2), and Fe^{III}-OCl/Ni^{II}-OCl species being mimics for haloperoxidases (chapter 6 and 7), are discussed.

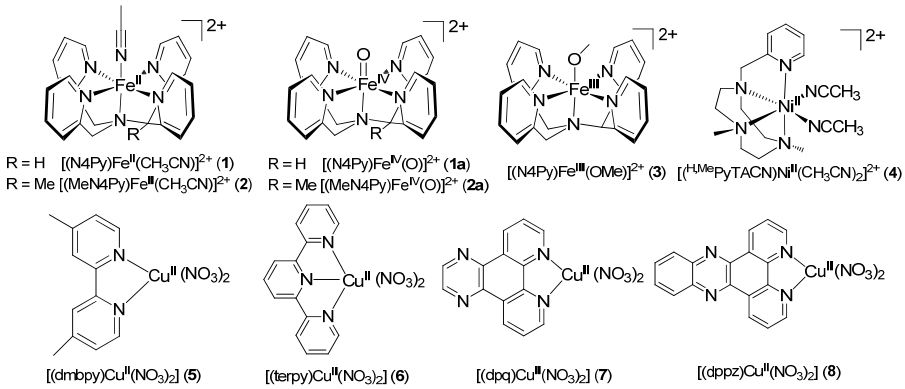


Figure 1 Structures of the complexes employed in this thesis.

When chemists refer to complexes as biomimetic, they generally mean that their systems are able to generate intermediates and, hence, catalyse chemical reactions similar to those carried out by the biological systems referred to. Generation of active intermediates, their characterisation by various spectroscopic techniques and

understanding their role in catalysis have direct relevance to understanding their role in biological systems. The synthesis and characterisation of several intermediates such as Fe^{IV}=O (chapter 4), Fe^{III}-OR (chapter 5), Fe^{III}-OCl (chapter 6), Ni^{II}-OCl and Ni^{II}-$O^{\cdot}$ (chapter 7) are discussed in this thesis. The multi-technique approach taken in this work allows for the detailed characterisation of several of these intermediates. In particular, Raman spectroscopy plays a pivotal role in the studies described here.

The aqueous chemistry of complexes **1** and **2** was explored extensively in chapter 2. A multi-technique approach was taken to establish the speciation of Fe^{II}(N4Py) complexes of relevance to DNA cleavage studies reported earlier.[2] Exchange of the ligand CH_3CN with aqua/hydroxido ligands occurs immediately upon dissolution of $[(N4Py)Fe^{II}(CH_3CN)]^{2+}$ in water. Moreover, depending on the pH, distinct species exist in aqueous solution and interchange reversibly with changes in pH. Furthermore, the pentadentate N4Py ligand is tetradentate at high pH. A further complication to speciation analysis of this system is that the complexes present in solution at equilibrium are a mixture of low and high spin states and show rapid spin interconversion. The equilibrium between singlet (low spin) and quintet (high spin) spin states in aqueous solution was proposed to be at the origin of the activity of Fe^{II}(N4Py) complexes in cleaving DNA with oxygen ($^3O_2$) as terminal oxidant, through the transient population of a triplet state.

The photo-induced oxidation of complexes **1** and **2** in various solvents (*i.e.* H_2O and MeOH) with oxygen as terminal oxidant is discussed in chapter 3. Interestingly, both complexes are photochemically inactive in acetonitrile, reflecting their high positive oxidation potentials (1.1 V *vs.* SCE). Irradiation with UV and visible light induces the oxidation of iron(II) complexes to the corresponding iron(III) complexes with oxygen as terminal oxidant. Moreover, the primary photoproduct of **2** in methanol is also photochemically active. Photochemical enhancement of the rate of oxidation of iron(II) complexes by oxygen ($^3O_2$) through outer sphere electron transfer was proposed. These results are important in understanding the photo enhanced cleavage of DNA with **1**. As mentioned above, the interconversion between the singlet and higher spin states would be expected to involve an intermediate triplet state, which would facilitate electron transfer to $^3O_2$, the first step in the cleavage of DNA by **1** with oxygen ($^3O_2$).

The photochemistry of iron complexes was extended further to the Fe^{IV}=O

complexes, which is the subject of chapter 5. In sharp contrast to **1** and **2**, complexes **1a** and **2a** show photochemical activity in acetonitrile. These complexes undergo photoreduction to the corresponding Fe^{II}-CH_3CN complexes under irradiation with UV and visible light (400 nm). Partial photoreduction to Fe(III) and to Fe(II) complexes was observed even in the solid state (dispersed in KCl) under irradiation with visible light. These photochemical properties were explored with respect for enhancing catalysis, *e.g.,* alkane hydroxylation and alkene epoxidation. The photochemical reduction of the Fe^{IV}=O complexes is faster in the presence of substrates such as ethyl benzene, benzyl alcohol, fluorene and indane. There are two steps involved in the photochemical process, the first step is the conversion of Fe^{IV}=O to Fe^{III}-OH/OR followed by a second photochemical step in which the Fe^{III}-OR converts to Fe^{III}-CH_3CN. This latter species is a powerful enough oxidant to oxidise Fe^{III}-OH/OR to the Fe^{IV}=O state and form the Fe^{II}-CH_3CN complex also. In addition, the Fe^{III}-OMe (**3**) complex is photochemically active in acetonitrile. In sharp contrast, the Fe^{III}-OH complex in acetonitrile is photochemically much less active. So the primary photoproduct in the reduction of Fe^{IV}=O is not an Fe^{III}-OH species, but instead an Fe^{III}-OR (R = alkyl) species. These data suggests that the C-H hydroxylation is via a rebound mechanism. The enhanced reactivity of Fe^{IV}=O species, under irradiation, towards substrate oxidation is attributed to the transient population of an S = 2 state.

Knowledge of the redox properties of Fe^{IV}=O species benefits the understanding of their reactivity towards substrate oxidation. Unfortunately, determination of the Fe^{IV}/Fe^{III} reduction potential by cyclic voltammetry is hampered by the sluggish rate of heterogeneous electron transfer encountered in the reduction. These problems are dealt with in depth in chapter 4. The chemical and electrochemical synthesis and characterisation of a non-heme Fe^{IV}=O species in water is reported. A clean conversion of complex **2** to **2a** in water was achieved electrochemically. In acetonitrile, conversion of complex **2** to **2a** was observed only in the presence of water. Moreover, the required potential (1.25 V *vs.* SCE) to generate the Fe^{IV}=O species is higher in acetonitrile compared to the value of (0.85 V *vs.* SCE) in water. This is attributed to the necessity of a high potential to oxidise Fe^{II}-CH_3CN to Fe^{III}-CH_3CN. Once Fe^{III}-CH_3CN is generated, immediate ligand exchange takes place to form Fe^{III}-OH_2, which oxidises to Fe^{IV}=O spontaneously at such high applied potentials. The available data suggested that the oxidation potential of the Fe^{IV}/Fe^{III} redox couple is around ~0.85 V, and not 0.41 V *vs.* SCE in water as concluded by Que and co-workers[3] for $[(N4Py)Fe^{IV}(O)]^{2+}$.

It has been proposed that in haloperoxidases a M-O-X (M = metal, X = Cl, Br and I) adduct is generated and is responsible for the halogenation of the substrates. Direct spectroscopic evidence for such intermediates had not yet been reported for any non-heme system. In chapter 6, the synthesis and spectroscopic characterisation of a non-heme Fe^{III}-OCl species is reported. Addition of aqueous NaOCl to acidic aqueous solutions of **1** or **2** at room temperature generates the corresponding Fe^{III}-OCl species. Over time the Fe^{III}-OCl species converts to the corresponding high valent Fe^{IV}=O species. Assignment of these intermediates was carried out by UV/Vis absorption, (resonance)Raman and EPR spectroscopy and by Cryo ESI-MS. Raman spectroscopic characterisation of the Fe^{III}-O and O-Cl modes was aided by bromine (Fe^{III}-O-Br) and with ^{18}O labelling. These intermediates react with styrene to yield the corresponding halohydrin and diol.

In chapter 7, generation of non-porphyrinic Ni^{II}-$O^{\cdot}$ and Ni^{II}-OCl species and their spectroscopic characterisation is described. Addition of aqueous NaOCl/$Ca(OCl)_2$ to an acetonitrile solution of **4** at room temperature generates a putative Ni^{II}-$O^{\cdot}$ species. Addition of Brønsted acids promotes the formation of such intermediates and increases the rate of their formation also. Characterisations of these intermediates were carried out with UV/Vis absorption, (resonance)Raman, NMR and EPR spectroscopy and by Cryo ESI-MS. The formation and loss of the Ni^{II}-$O^{\cdot}$ species was followed by (resonance)Raman spectroscopy. Formation of the Ni^{II}-$O^{\cdot}$ species was confirmed by Raman spectroscopy, again with the use of bromine and with ^{18}O labelling and evidence for the formation of Ni^{II}-OCl species was obtained by Cryo ESI-MS. The former species is proposed to activate C-H bonds and the latter species is proposed to insert the halogen into the substrate. To the best of my knowledge, this is the first direct spectroscopic evidence for the involvement of Ni^{II}-$O^{\cdot}$ and Ni^{II}-OCl species in catalysing the halogenation of aliphatic moieties.

Complexes **5** to **8** catalyse enantioselective C-C bond forming reactions in water with DNA as the source of chirality. Complex **5** provides the highest enantioselectivities in DNA-based asymmetric catalysis, whereas complex **6** yields the opposite enantiomer.[4] In chapter 8, the interaction with DNA of a series of Cu(II) polypyridyl complexes was studied by various spectroscopic techniques in the absence of substrate. For the first time UV resonance Raman spectroscopy was employed to probe the interaction of Cu(II) complexes with DNA. In the presence of DNA, complexes **7** and **8**, which are intercalators, show clear shifts in their

Raman spectrum whereas the groove binder **5** does not. These spectroscopic observations point out those complexes that induce the highest *ee* in DNA-based asymmetric catalysis are primarily groove binders. These findings provide important insights into the complex structure of these DNA-based catalysts and set the stage for establishing the effect of substrates on the interaction between DNA and the complexes.

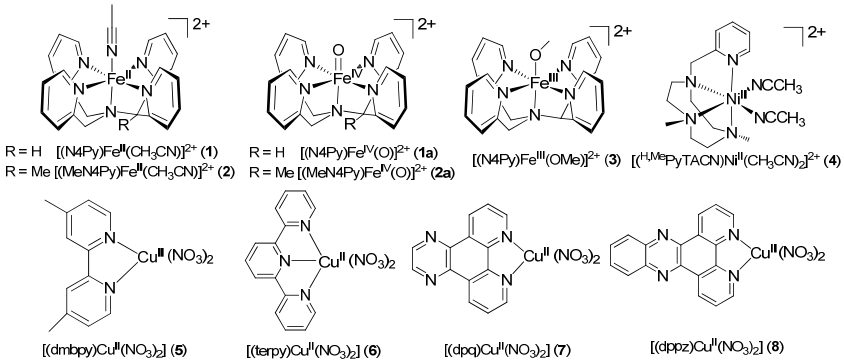
Finally in chapter 9 the work described in the thesis is placed in perspective.

References

(1) (a) J. Steinreiber, T. R. Ward, *Coord. Chem. Rev.*, **2008**, *252*, 751-766; (b) V. Köhler, Y. M. Wilson, C. Lo, A. Sardo, T. R. Ward, *Curr. Opin. Biotech.*, **2010**, *21*, 744-752; (c) A. J. Boersma, R. P. Megens, B. L. Feringa, G. Roelfes, *Chem. Soc. Rev.*, **2010**, *39*, 2083-2092.
(2) (a) Q. Li, W. R. Browne, G. Roelfes, *Inorg. Chem.*, **2010**, *49*, 11009-11017; (b) Q. Li, W. R. Browne, G. Roelfes, *Inorg. Chem.,* **2010**, *50*, 8318-8325.
(3) D. Wang, M. Zhang, P. Bühlmann, L. Que, Jr., *J. Am. Chem. Soc.*, **2010**, *132*, 7638-7644.
(4) (a) G. Roelfes, A. J. Boersma, B. L. Feringa, *Chem. Commun.*, **2006**, 635-637; (b) A. J. Boersma, J. E. Klijn, B. L. Feringa, G. Roelfes, *J. Am. Chem. Soc.,* **2008**, *130*, 11783-11790.

Samenvatting

Vele chemische omzettingen waar chemici in het laboratorium mee worstelen worden door natuurlijke systemen vaak uitgevoerd met hogere activiteit, betere selectiviteit en onder vorming van biologisch afbreekbare bijproducten. In scherpe tegenstelling tot biologische systemen, lijden de door mensen gemaakte structurele en functionele modellen van biologische systemen aan een ernstig gebrek aan reactiviteit en selectiviteit in de door hun gekatalyseerde reacties. Het evenaren van de capaciteiten van biologische systemen met modellen in het laboratorium is een op het eerste gezicht onmogelijke taak. In biologische systemen zijn complexe structuren betrokken bij het uitvoeren van chemische reacties; in enzymen vinden de chemische reacties bijvoorbeeld plaats in het zogenaamde actieve centrum. Naast het actieve centrum vormt een enzym een secundaire coordinatie-omgeving. Dit helpt om een betere selectiviteit van de gekatalyseerde chemische reactie te verkrijgen aangezien hierdoor het substraat bij voorkeur maar in één orientatie in het actieve centrum past. Deze voordelen zijn niet gemakkelijk te bewerkstelligen in een biomimetisch systeem. Het is echter in een aantal biomimetische systemen gelukt om een gedefinieerde secundaire coordinatie omgeving te creëren.[1] Een van deze systemen vormt het onderwerp van hoofdstuk 8, hoewel de katalytische reacties zelf daar niet beschreven worden. In dit proefschrift worden een aantal biomimetische systemen beschreven, waaronder een serie Fe^{II}-N4Py complexen (Figuur 1) die functionele modellen zijn voor Fe^{II}-BLM (BLM = bleomycine) (hoofdstuk 2) en Fe^{III}-OCl/Ni^{II}-OCl deeltjes die model staan voor haloperoxidasen (hoofdstuk 6 en 7).



Figuur 1 De structuren van de complexen die in dit proefschrift beschreven worden.

Wanneer chemici complexen biomimetisch noemen, dan bedoelen ze in het algemeen dat ze in staat zijn om met hun systemen intermediairen te genereren en

dat deze, dientengevolge, chemische reacties kunnen katalyseren die normaliter uitgevoerd worden door de nagebootste biologische systemen. Het genereren van actieve intermediairen, de karakterisatie ervan met behulp van diverse spectroscopische technieken en het begrijpen van hun rol in de katalyse zijn direct van belang met betrekking tot het begrijpen van hun rol in biologische systemen. De synthese en karakterisatie van diverse intermediairen zoals Fe^{IV}=O (hoofdstuk 4), Fe^{III}-OR (hoofdstuk 5), Fe^{III}-OCl (hoofdstuk 6), Ni^{II}-OCl en Ni^{II}-$O^{\cdot}$ (hoofdstuk 7) worden in dit proefschrift beschreven. De in dit proefschrift genomen benadering, dat wil zeggen gebruikmakend van een groot aantal technieken, heeft geresulteerd in de gedetailleerde karakterisatie van een aantal van deze intermediairen. Met name Ramanspectroscopie speelt een cruciale rol in het onderzoek dat beschreven wordt in dit proefschrift.

Het onderzoek van de chemie in water van de complexen **1** en **2** wordt uitgebreid beschreven in hoofdstuk 2. Door gebruik te maken van een groot aantal technieken was het mogelijk om vast te stellen welke Fe^{II}(N4Py) complexen relevant zijn in verband met eerdere studies hiermee met betrekking tot het knippen van DNA.[2] Uitwisseling van het CH_3CN ligand met water/hydroxido liganden vindt meteen plaats als $[(N4Py)Fe^{II}(CH_3CN)]^{2+}$ opgelost wordt in water. Afhankelijk van de pH zijn er bovendien duidelijk verschillende deeltjes in water te onderscheiden en deze deeltjes kunnen reversibel in elkaar overgaan als gevolg van veranderingen in de pH. Tevens treedt het, in principe, pentadentaat ligand N4Py bij hoge pH op als tetradentaat ligand. Een verdere complicatie bij het analyseren van welke deeltjes in evenwicht aanwezig zijn in dit systeem is dat de in oplossing aanwezige complexen in zowel lage als hoge spintoestand voorkomen en dat deze snel in elkaar overgaan. Er wordt gepostuleerd dat het evenwicht tussen de singlet (lage spin) en quintet (hoge spin) spintoestanden in oplossingen van Fe^{II}(N4Py) in water ten grondslag ligt aan de activiteit van Fe^{II}(N4Py) complexen met betrekking tot het knippen van DNA met zuurstof ($^3O_2$) als oxidator, via de tijdelijke populatie van een triplet toestand.

In hoofstuk 3 wordt de foto-geïnduceerde oxidatie van de complexen **1** en **2** in diverse oplosmiddelen (*i.e.* H_2O en MeOH) met zuurstof als uiteindelijk oxidant beschreven. Het is interessant dat beide complexen niet fotochemisch actief zijn in acetonitril, hetgeen weerspiegeld wordt door hun hoge positieve oxidatie potentiaal (1.1 V *vs.* SCE). Bestraling met UV en zichtbaar licht brengt de oxidatie van de ijzer(II) complexen naar de corresponderende ijzer(III) complexen teweeg waarbij

zuurstof als uiteindelijke oxidator optreedt. Bovendien is het primaire fotoproduct van complex **2** in methanol ook fotochemisch actief. De fotochemische versnelling van de oxidatiesnelheid van ijzer(II) complexen door zuurstof ($^3O_2$) door middel van 'outer sphere' elektronen-overdracht wordt gepostuleerd. Deze resultaten zijn van belang om de versnelling van het knippen van DNA door **1** met behulp van licht te kunnen begrijpen. Zoals hierboven vermeld wordt, valt het te verwachten dat er bij de overgang tussen de singlet en de hogere spintoestanden een triplet toestand als intermediair betrokken is, hetgeen elektronoverdracht naar $^3O_2$, de eerste stap in het knippen van DNA door **1** met zuurstof ($^3O_2$), mogelijk zou maken,

De fotochemie van ijzer complexen is verder uitgebreid naar de Fe^{IV}=O complexen, hetgeen het onderwerp is van hoofdstuk 5. In scherpe tegenstelling tot **1** en **2**, laten de complexen **1a** en **1b** fotochemische activiteit zien in acetonitril. Deze complexen ondergaan foto-reductie naar de corresponderende Fe^{II}-CH_3CN complexen als ze bestraald worden met UV en zichtbaar licht (400 nm). Gedeeltelijke foto-reductie naar Fe(III) en naar Fe(II) complexen door middel van bestraling met zichtbaar licht werd zelfs in vaste toestand (als dispersie in KCl) gezien. De fotochemische eigenschappen met betrekking tot het versnellen van de katalyse, bijvoorbeeld de hydroxylering van alkanen en de epoxidatie van alkenen, werd onderzocht. De fotochemische reductie van de Fe^{IV}=O complexen verloopt sneller in de aanwezigheid van substraten zoals ethylbenzeen, benzylalcohol, fluoreen en indaan. Er zijn twee stappen betrokken in het fotochemische proces: de eerste stap is de overgang van Fe^{IV}=O naar Fe^{III}-OH/OR en dit wordt gevolgd door een tweede fotochemische stap waarin Fe^{III}-OR omgezet wordt in Fe^{III}-CH_3CN. Dit laatste deeltje is een voldoende sterke oxidator om Fe^{III}-OH/OR te oxideren naar Fe^{IV}=O en hierbij wordt tevens het Fe^{II}-CH_3CN complex gevormd. Ook het Fe^{III}-OMe (**3**) complex is fotochemisch actief in acetonitril. Het Fe^{III}-OH complex is daarentegen fotochemisch veel minder actief in acetonitril. Het primaire fotoproduct van de reductie van Fe^{IV}=O is dus niet een Fe^{III}-OH deeltje maar een Fe^{III}-OR (R = alkyl) deeltje. Deze gegevens suggereren dat de C-H oxidatie plaatsvindt via een zogenaamd 'rebound mechanisme'. De door bestraling verhoogde reactiviteit van Fe^{IV}=O met betrekking tot het oxideren van substraten wordt toegeschreven aan de tijdelijke populatie van een S = 2 toestand.

Kennis van de redox eigenschappen van Fe^{IV}=O deeltjes is van belang om de reactiviteit van deze deeltjes met betrekking tot de oxidatie van substraten te begrijpen. Helaas wordt het vaststellen van de Fe^{IV}/Fe^{III} reductie potentiaal door

middel van cyclovoltammetrie belemmerd door de traagheid van de heterogene elektronenoverdracht die optreedt bij de reductie. Deze problemen worden uitgebreid behandeld in hoofdstuk 4. De chemische en electrochemische synthese en karakterisatie van een niet-heem Fe^{IV}=O deeltje in water wordt beschreven. Complex **2** kan in water electrochemisch omgezet worden naar complex **2a**. In acetonitril werd de omzetting van complex **2** in **2a** alleen gezien in de aanwezigheid van water. Bovendien was de benodigde potentiaal om het Fe^{IV}=O deeltje te genereren hoger in acetonitril (1.25 V *vs.* SCE) dan in water (0.85 V *vs.* SCE). Dit wordt toegeschreven aan de vereiste dat een hoge potentiaal nodig is om Fe^{II}-CH_3CN te oxideren naar Fe^{III}-CH_3CN. Zodra Fe^{III}-CH_3CN is gegenereerd vindt onmiddelijk ligand uitwisseling plaats resulterend in de vorming van Fe^{III}-OH_2 en dit deeltje wordt spontaan geoxideerd naar Fe^{IV}=O onder dergelijk hoge toegepaste potentialen. De beschikbare data suggereert dat de oxidatie potentiaal van het het Fe^{IV}/Fe^{III} redox-koppel in water rond ~0.85 V ligt en niet rond 0.41 V *vs.* SCE, zoals geconcludeerd wordt door Que *et al.*[3] voor $[(N4Py)Fe^{IV}(O)]^{2+}$.

Het is voorgesteld dat een M-O-X (M = metaal, X = Cl, Br en I) adduct gegenereerd wordt in haloperoxidasen en dat dit deeltje verantwoordelijk is voor de halogenering van de substraten. Direct spectroscopisch bewijs voor het bestaan van dergelijke intermediairen is tot dusver nog niet gerapporteerd voor niet-heem systemen. In hoofdstuk 6 wordt de synthese en spectroscopische karakterisatie van een niet-heem Fe^{III}-OCl deeltje behandeld. Door toevoeging van een oplossing van NaOCl in water aan zure oplossingen van **1** en **2** in water wordt bij kamertemperatuur het corresponderende Fe^{III}-OCl deeltje gevormd. Na verloop van tijd verandert het Fe^{III}-OCl deeltje in het corresponderende hoog-valente Fe^{IV}=O deeltje. De karakterisatie van deze intermediairen is uitgevoerd met behulp van UV/Vis absorptie-, (resonantie) Raman- en EPR-spectroscopie en met cryo ESI-MS. Bij de toekenning van de Fe^{III}-O en O-Cl pieken in de Ramanspectra werd gebruik gemaakt van labelling met broom (Fe^{III}-O-Br) en ^{18}O. Deze intermediairen reageren met styreen onder vorming van het corresponderende halohydrine en het diol.

In hoofdstuk 7 wordt de vorming en de spectroscopische karakterisatie van niet-porphyrine Ni^{II}-$O^{\cdot}$ en Ni^{II}-OCl deeltjes beschreven. Bij kamertemperatuur zorgt toevoeging van een oplossing van $NaOCl/Ca(OCl)_2$ in water aan een oplossing van **4** in acetonitril voor de vorming van, vermoedelijk, een Ni^{II}-$O^{\cdot}$ deeltje. De toevoeging van Brønsted-zuren bevorderd de vorming van dergelijke intermediairen

en versneld tevens de vorming ervan. De karakterisatie van deze intermediairen werd uitgevoerd met behulp van UV/Vis absorptie-, (resonantie) Raman-, NMR- en EPR-spectroscopie en met cryo ESI-MS. Zowel de vorming als het verdwijnen van het Ni^{II}-O· deeltje werd gevolgd met behulp van (resonantie) Ramanspectroscopie. De formatie van het Ni^{II}-O· deeltje werd bevestigd met Ramanspectroscopie, wederom met behulp van labelling met broom en ^{18}O, en bewijs voor de vorming van het Ni^{II}-OCl deeltje werd verkregen door middel van cryo ESI-MS. Er wordt gepostuleerd dat het eerstgenoemde deeltje C-H bindingen activeert en dat het laatstgenoemde deeltje verantwoordelijk is voor de insertie van een halogeen in het substraat. Voor zover mij bekend is is dit het eerste directe spectroscopische bewijs voor de betrokkenheid van Ni^{II}-O· en Ni^{II}-OCl deeltjes bij de gekatalyseerde halogenering van alifatische verbindingen.

De complexen **5** en **8** katalyseren de enantioselectieve vorming van C-C bindingen in water waarbij DNA de bron van de chiraliteit is. Complex **5** zorgt voor de hoogste enantioselectiviteit in DNA-gebaseerde asymmetrische katalyse, terwijl bij gebruik van complex **6** het tegenovergestelde enantiomeer verkregen wordt.[4] In hoofdstuk 8 wordt de interactie van een serie Cu(II) polypyridyl complexen met DNA in de afwezigheid van substraten bestudeerd met behulp van diverse spectroscopische technieken. Voor het eerst is er gebruik gemaakt van UV resonantie Ramanspectroscopie om de interactie van Cu(II) complexen met DNA te onderzoeken. In de aanwezigheid van DNA laten de intercalerende complexen **7** en **8** duidelijke verschuivingen zien in hun Ramanspectra, terwijl dit niet het geval is bij complex **5**, dat in de groeve van het DNA bindt. Het spectroscopische bewijs duidt erop dat de complexen die de hoogste *ee* geven in de DNA-gebaseerde asymmetrische katalyse voornamelijk binden in de groeve van het DNA. Deze bevindingen geven belangrijke inzichten in de complexe structuur van deze DNA-gebaseerde katalysatoren en zijn een belangrijke basis voor het vaststellen van het effect van de substraten op de interactie tussen DNA en de complexen.

Tenslotte wordt in hoofdstuk 9 het werk dat in dit proefschrift beschreven wordt in perspectief geplaatst.

Referenties

(1) J. Steinreiber, T. R. Ward, *Coord. Chem. Rev.*, **2008**, *252*, 751-766; (b) V. Köhler, Y. M. Wilson, C. Lo, A. Sardo, T. R. Ward, *Current Opinion in Biotech.*, **2010**, *21*, 744-752; (c) A. J. Boersma, R. P. Megens, B. L. Feringa, G. Roelfes, *Chem. Soc. Rev.*, **2010**, *39*, 2083-2092.

(2) (a) Q. Li, W. R. Browne, G. Roelfes, *Inorg. Chem.*, **2010**, *49*, 11009-11017; (b) Q. Li, W. R. Browne, G. Roelfes, *Inorg. Chem.,* **2010**, *50*, 8318-8325.

(3) D. Wang, M. Zhang, P. Bühlmann, L. Que, Jr., *J. Am. Chem. Soc.*, **2010**, *132*, 7638-7644.

(4) (a) G. Roelfes, A. J. Boersma, B. L. Feringa, *Chem. Commun.*, **2006**, 635-637; (b) A. J. Boersma, J. E. Klijn, B. L. Feringa, G. Roelfes, *J. Am. Chem. Soc.,* **2008**, *130*, 11783-11790.

సారాంశము

మన నిత్యజీవితంలో నిరంతరం ఎన్నో రసాయన చర్యలు మన ప్రమేయం లేకుండానే జరుగుతాయి. ఈ రసాయన చర్యలను ప్రకృతిలోని జీవనిర్మాణాలు అత్యంత సూక్ష్మనిర్మాణాలైన ఎంజైమ్ లు మరియు ప్రోటీనుల సహాయంతో ఎటువంటి హానికరమైన వ్యర్థ పదార్థాలను విడుదల చేయకుండా నిర్వహిస్తాయి. ఈ చర్యలలో వివిధ రకములైన లోహాలు పాల్గొంటాయి. ఉదాహరణకు కిరణజన్యసంయోగక్రియలో 'మాంగనీస్' అనే లోహము నీటిని, ఆక్సిజన్ మరియు హైడ్రోజన్ గా మార్చే శక్తిని విడుదల చేస్తుంది. చాలా మంది రసాయన శాస్త్రవేత్తలు ప్రకృతిలో ఇటువంటి జీవ నిర్మాణాల నుండి ప్రేరణపొంది, అటువంటి నిర్మాణాలను ప్రయోగశాలల్లో అనుకరించి, వాటి సహాయంతో రసాయన చర్యలను ఉత్ప్రేరణ చెయ్యడానికి కలలు కంటారు. కానీ ఇప్పటివరకు ఏ ఒక్క జీవ నిర్మాణాన్ని ఖచ్చితంగా ప్రయోగశాలల్లో ఏ రసాయన శాస్త్రవేత్త అనుకరించలేదు. దీనికి గల కారణం ప్రకృతి ఉపయోగించే సంక్లిష్టమైన నిర్మాణాలను ప్రయోగశాలల్లో తయారు చెయ్యడం కష్టసాధ్యము. కానీ శాస్త్రవేత్తలు అనుకరించిన కొన్ని జీవాణుకరణులు మంచి ఉత్ప్రేరకాలుగా పనిచేసి ఆశాజనకమైన ఫలితాలను ఇస్తున్నాయి. ఇటువంటి కొన్ని జీవాణుకరణులను (ఉత్ప్రేరకాలను) ఈ పరిశోధనలో భాగంగా జరిగింది. ఉదాహరణకు ఐరన్ (II) - N4py అనే సంశ్లిష్ట సమ్మేళనం ఐరన్(II) - బ్లుయోమైసిన్ అనే జీవ నిర్మాణానికి ఒక అనుకరణ. ఈ జీవాణుకరణులను అధ్యయనం చేసిన ఫలితాల ఆధారంగా ఆ జీవ నిర్మాణాల పనితీరును అర్థం చేసుకోవడానికి కృషి చేస్తున్నాము.

ఈ పరిశోధనలో భాగంగా ఐరన్(II) రసాయన లక్షణాలను మరియు వాటి యొక్క స్పిన్ సమతాస్థితులను నీరు మరియు ఎసిటోనైట్రేట్ ద్రావణాలలో అధ్యయనం చేయడం జరిగింది. ఈ ఫలితాల ఆధారంగా ఈ సమ్మేళనాలు ఆక్సిజన్ తో చర్య నొందుటకు స్పిన్ సమతాస్థితి ఎంతో దోహదం చేస్తుందనీ నిర్ధారించితిమి. ఈ పుస్తకం లో వివరించిన మిగిలిన వివిధ పరిశోధనలకు ఎంతో ఉపయోగపడ్డాయి. ఈ ఐరన్ (II) రసాయన సమ్మేళనాలు ఆక్సిజన్ సమక్షంలో జన్యువులను నాశనం చెయ్యడం ద్వారా క్యాన్సర్ ను నిర్మూలిస్తాయి. ఈ చర్యను కాంతి సమక్షంలో మరింత సమర్థవంతంగా జరుగుతాయనీ ఈ మధ్యకాలంలో కనుగొనడం జరిగింది. దీనికి కారణం తెలుసుకునేందుకు ఈ ఐరన్(II) సమ్మేళనాల కాంతి రసాయన చర్యలను వేర్వేరు ద్రావణాలలో అధ్యయనం చేయడం జరిగింది. ఈ ఫలితాలను అధ్యయనం – 3 లో విశదీకరించాను. కాంతి సమక్షంలో ఈ ఐరన్(II) రసాయన సమ్మేళనాలు ఆక్సీకరణం చెంది ఐరన్(II) సమ్మేళనాలను ఏర్పరుస్తాయి. ఈ కాంతి రసాయన చర్యలకు ముఖ్యకారణం నీటిలో గల స్పిన్ సమతాస్థితి కారణంగానే ఈ ఐరన్(II) సమ్మేళనాలు ఆక్సిజన్ తో సమర్థవంతంగా చర్య నొంది జన్యువులను నాశనం చెయ్యడం ద్వారా క్యాన్సర్ ను నిర్మూలిస్తాయని నిర్ధారించితిమి.

అదే విధంగా వివిధ చర్యామాధ్యమాలు ఉదాహరణకు ఐరన్(IV) సమ్మేళనాల యొక్క కాంతి రసాయన చర్యలను ఉపయోగించి అనేక రసాయన చర్యలను వేగవంతం చేయడం జరిగింది. అంతే కాకుండా మరికొన్ని చర్యామాధ్యమాలను బ్లీచింగ్ పౌడర్ నీటిని ఐరన్(II) సమ్మేళనాలకు కలపడం ద్వారా తయారు చేయడం జరిగింది. ఈ చర్యా మాధ్యమాలను ఉపయోగించి అనేక రసాయన చర్యలను సమర్థవంతంగా ఉత్ప్రేరణ చేయడం జరిగింది.

చివరిగా ఈ పరిశోధనలను కాపర్(II) సమ్మేళనాలు మరియు జన్యువుల మధ్య చర్యను అవగాహన చేసుకోవడంపై దృష్టి పెట్టడం జరిగింది. ఈ పరిశోధనా ఫలితాలు, కష్టతరమైన ఉత్ప్రేరణ చర్యలను అర్థం చేసుకోవడానికి ఉపయోగపడతాయని భావిస్తునాను. చివరిగా ఈ పరిశోధనలో నిర్మించిన ఎన్నో జీవాణుకరణులు మరియు వాటి నుండి తయారు చేసిన రసాయన మాధ్యమాల జీవనిర్మాణాలను మరియు వాటి యొక్క పనితీరును విజయవంతంగా పూర్తి చేయడం జరిగింది.

– అప్పారావు ద్రాక్షారపు.

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